

IN THE CLAIMS:

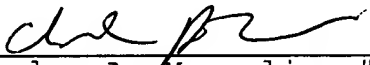
Cancel claims 19 and 23.

REMARKS

The present amendment is submitted to remove reference to the improvement of physiological responses in a mammal such as oxygen consumption.

Respectfully submitted,
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CAM:ds
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METHOD FOR PREVENTION OF ULCERS

FIELD OF THE INVENTION

The present invention provides a method for the prevention of ulcers in animals, including horses, dogs and humans.

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BACKGROUND

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The development of endoscopes able to visualize the stomach of horses showed that the frequency of gastric ulcers in horses is higher than presumed. The aetiology of gastric ulcers in horses is not well known but it is assumed that stress plays an important role in some cases.

It is well-known to treat gastric ulcers in horses and foals by the administration of a proton pump inhibitor which is preferably 5-metoxo-2-[[[4-metoxo-3,5-dimethyl-2-pyridinyl)methyl]sulphanyl]-1H-benzimidazole, whose common name is Omeprazole. A paste for horses containing 37% w/w. Omeprazole is marketed under the trade name Gastrogard for the treatment of ulcers. Generally, this paste is to be administered orally once a day for 4 weeks at the dosage of 1.8 mg omeprazole/lb body weight (4 mg/kg). Thereafter, recurrence of gastric ulcers can be prevented if the treatment is continued for at least an additional 4 weeks at a lower dose of 0.9 mg/lb (2 mg/kg).

Proton pump inhibitors (PPI) are potent inhibitors of gastric acid secretion by inhibiting H^+K^+ -ATPase, the enzyme involved in the final step of hydrogen ion production in the parietal cells.

The PPI omeprazole is disclosed in US patent No. 4 255 432.

Pharmaceutical compositions containing proton pump inhibitors are also disclosed in the PCT Patent Application WO 96/31213 and US Patent No. 5708017 which discloses a stable, ready-to-use oral paste composition of proton pump inhibitor, such as, for example, omeprazole.

Another oral composition containing a proton pump inhibitor is known from WO 94/25070 in the form of enteric coated dry particles mixed with a dry gelling agent.

For a good review of the diagnostic and treatment of equine gastric ulcer syndrome (EGUS) or gastrointestinal ulcers, see EQUINE VETERINARY EDUCATION (1999) 11 (5) 262-272.

While treatment of ulcers and prevention of recurrence of the treated ulcers is known and is efficient, no method of prevention of ulcers, including gastric ulcers in animals, including horses and dogs where ulcers are relatively frequent, is known and it was believed that such prevention would be very difficult. Moreover, the far insufficient knowledge of the aetiology of the ulcers added to the difficulty of conceiving a method able to prevent occurrence of ulcers in animals.

OBJECTS AND SUMMARY OF THE INVENTION

The present invention provides a method for the prevention of gastric ulcers, such as gastrointestinal ulcers in a mammal, e.g. a domestic mammal, a farm mammal, a companion mammal, a game or sport mammal, such as horses, dogs, humans, and other mammals that may be susceptible to such ulcers. The method comprises administering e.g., periodically, an effective amount of a proton pump inhibitor to the mammal. The administration can be prior to or during a stressful event. It can also be a single treatment or administration over one or two days. This administering can be of amounts used in animals for the treatment of ulcers, although lower or higher doses can also be employed.

This prevention of gastric ulcers is in mammals prior to the occurrence of a gastric ulcer condition and is in contrast to treatment or prevention of reoccurrence in an animal that has already had a gastric ulcer condition.

The invention also provides the use of a proton pump inhibitor, preferably omeprazole, for the preparation of a formulation for the prevention of gastric ulcers in mammals, ~~and/or improving physiological responses in a mammal.~~

formulations are disclosed in PCT Patent WO 96/31213 and US Patent N°5 708 017 which are hereby incorporated by reference.

Other oral formulations can be made in the form of enteric dry particles mixed with a dry gelling agent.

5 The following formulations are preferred for humans: oral solutions or suspensions, gels, tablets, capsules or powder.

 The efficiency of the method for preventing significant or persistent ulceration was completely unexpected. ~~Further it was discovered~~ that this method improves physiological responses in mammals such as
10 horses, e.g. oxygen consumption and time to fatigue, and thus, the present invention envisions methods for improving oxygen consumption and/or time to fatigue comprising administering to a mammal a PPI as herein discussed, e.g., for prevention of ulcers (e.g. such as administration of PPI on continuous
15 ~~basis~~).

 The invention also provides the use of a proton pump inhibitor, preferably omeprazole, for the preparation of a formulation for the prevention of gastric ulcers in mammals, ~~and/or for improving physiological responses in a~~
20 ~~mammal~~.

 It also provides formulations prepared according to said use and comprising an amount of PPI which is less, preferably 50%, than the usual
25 dose for preventing ulcers for the same mammal.

 The invention will be further described in the following non limiting examples.

EXAMPLES

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 The following exemplifies a comparative method showing the efficiency of a formulation according to the invention for the prevention of gastric ulcers in horses.

 Example 1: Preparation of an omeprazole-containing oral paste
30 for horses.

 The paste for horses, containing 37% w/w omeprazole can be prepared according to US Patent N° 5 708 017. This paste is contained in adjustable-dose syringes for oral delivery.